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Dichloro(1,2-diaminocyclohexane) Platinum(II) (DACHPt)-Loaded Gold Nanoshells for Chemo-Photothermotherapy of Colorectal Cancer

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Extended Abstract

Oxaliplatin is a third-generation platinum chemotherapeutic that has been applied as a first-line treatment for the advanced colorectal cancer and as a primary therapy for other malignancies such as gastrointestinal, lung, breast, and ovarian cancers. However, the majority of patients treated with oxaliplatin would suffer from neurotoxic side effects including the chronic painful sensory neuropathy and an acute transient syndrome such as paresthesia in limbs and perioral region that usually occur right after infusion [1]. The oxaliplatin-induced neuropathy results in drug reduction and cessation, which can increase cancer therapy-related mortality. In this regard, the use of nanoscale drug delivery systems may be a potential solution to decrease the adverse side effects and improve the efficacy of platinum chemotherapeutic drugs.

In the present study, we utilize a micellar template-based gold nanoshell as a platform to deliver the platinum-based drug, dichloro(1,2-diaminocyclohexane)platinum(II) (DACHPt), in which the gold nanoshells not only work as a drug delivery system but also provide a remarkable photothermal effect resulting in a synergistically combined chemo-photothermotherapy. Due to its stable structure, tunable resonance and excellent photothermal conversion efficiency, gold nanoshell is a potential candidate for biomedical applications. Here, the micellar core of gold nanoshells was prepared using poly[2-(N,N-dimethylamino)ethyl methacrylate]-poly(ε-caprolactone) (PDMA-PCL) amphiphilic copolymers based on our recent study [2]. PDMA-PCL copolymers could self-assemble into micelles at a low critical micelle concentration (CMC) and displayed a high DACHPt encapsulation efficiency. With the positive surface charge from the outstretched hydrophilic PDMA segments, chloroauric anions were attracted to the PDMA-PCL micellar surface and subsequently reduced into gold atoms *in situ*, forming gold shell layers. This gold nanoshell on the micellar surface can function as a diffusion barrier which reduces premature drug release. Then, the as-prepared gold nanoshells are pegylated to enhance the biocompatibility and prolong the circulation time. The DACHPt-loaded gold nanoshells have an average hydrodynamic diameter around 200 nm and possess a broad surface plasmon resonance band in the absorption spectrum and a high photothermal conversion ability. The *in vitro* studies show that gold nanoshells are highly biocompatible and can lead to a significant temperature increase that is high enough to ablate tumor cells upon exposure to NIR laser irradiation at a moderate power density (1 W cm^{-2}). Furthermore, with the release of the loaded platinum chemotherapeutic drug, the DACHPt-loaded gold nanoshells exhibit a better anticancer effect by exploiting the synergistic effects from combined chemo-phtothermotherapy, comparing to that of the single therapy such as chemotherapy or photothermal therapy alone. With the established DACHPt-loaded gold nanoshells and the combination of photothermal therapy and chemotherapy, we aim to achieve an efficient curative colorectal cancer therapy by eliminating cancer cells and decrease the neurotoxic side effects that are usually observed clinically after the use of platinum chemotherapeutics.

References

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